

Selected Aspects of the Neuroimmunology of Cell Therapies for Neurologic Disease

Perspective

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Abstract

Neurologic disease remains a cause of incalculable suffering, a formidable public health burden, and a wilderness of complex biology and medicine. At the same time, advances in basic science, technology, and the clinical development toolkit bring meaningful benefit for patients along with realistic hope for those whose conditions remain inadequately treated. This perspective focuses on cell-based therapies for neurologic disease, with particular emphasis on neuro-immunologic disorders and on the immunologic considerations of cell therapy for nonimmune conditions. I will consider the use of chimeric antigen receptor (CAR)-T effector cells and regulatory T-cell therapies for autoimmune conditions. I will briefly discuss the immune aspects of pluripotent stem cell (PSC)-derived neuronal therapies. With apologies for the omission, we do not discuss mesenchymal stem cells, glial progenitor cells, or CAR-NK cells, primarily for space limitations.

Cell therapies rank among the more impressive technological and clinical advances in contemporary medical research. Their main practical effect has been exerted in treating hematologic malignancy, with particular efficacy in B-cell tumors such as acute lymphoblastic leukemia, lymphoma, and myeloma.¹ As a natural evolution, this therapeutic approach was extended to autoimmune conditions implicating B cells, including those that affect the central and peripheral nervous systems.^{1–4} Last year, the topic was authoritatively reviewed in this journal.^{5,6} In part, the present article seeks to build on, and update, those publications.

CAR-T Cells

CAR-T cells use antigen recognition elements derived from immunoglobulins (Igs) and expressed as single-chain fragment variable (scFv) constructs, which incorporate the antigen-recognition domains of Ig heavy and light chains as fusion proteins that are engineered to fold, so as to enable high-affinity binding to antigenic targets. For expression at the plasma membrane, CAR-T constructs include transmembrane domains. Signaling competence of scFv in CAR-T cells is endowed by coupling to the CD3- ζ chain, with addition of the intracellular components of costimulatory elements such as CD137/4-1BB. Together, this engineering affords CAR-T cells with high-affinity antigen recognition and downstream signaling that confers proliferative capacity, effector function, and persistence in the recipient for the durable therapeutic effect. Similar to immunoglobulin, the CAR-T receptor is not limited by MHC restriction for antigen recognition.

The role of B cells in multiple sclerosis (MS), once rather neglected, has become an unavoidable topic, in substantial part due to unexpected, dramatic success treating relapsing pathology of MS with CD20 antibodies.⁷ After decades of effort, the multiplicity of functions of B cells in MS remains under investigation because the canonical property—antibody

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Clinical Aspects Of Neuroimmunology

A Gutmann



Clinical Aspects Of Neuroimmunology:

The book delves into Clinical Aspects Of Neuroimmunology. Clinical Aspects Of Neuroimmunology is a crucial topic that must be grasped by everyone, from students and scholars to the general public. This book will furnish comprehensive and in-depth insights into Clinical Aspects Of Neuroimmunology, encompassing both the fundamentals and more intricate discussions.

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